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# A Phase 2 Study of Ianalumab in Patients With Primary Immune Thrombocytopenia Previously Treated With At Least Two Lines of Therapy (VAYHIT3)

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# Disclosures

**Dr. Charlotte Bradbury**

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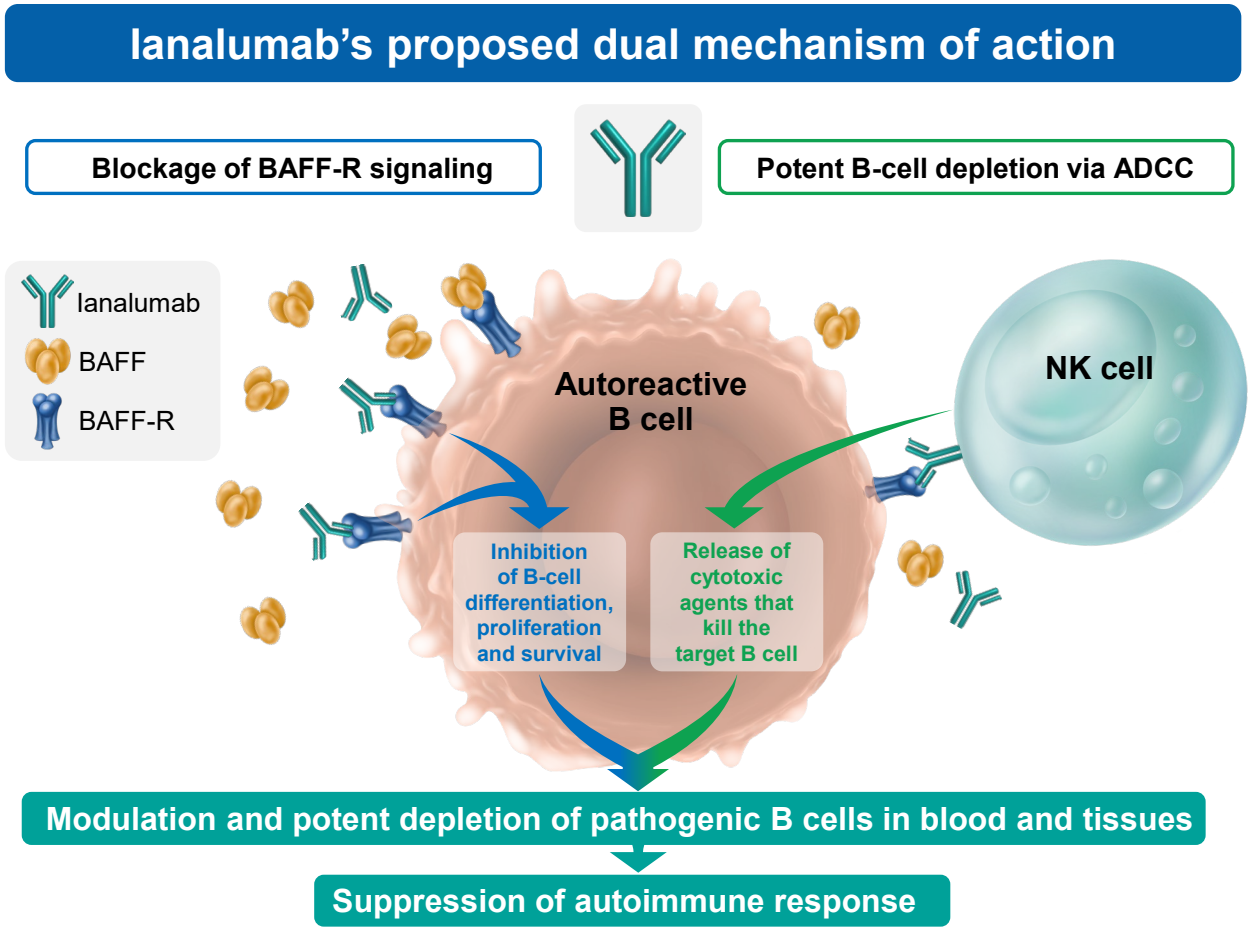
# Introduction

- The BAFF signalling pathway is crucial for B-cell proliferation, differentiation and survival, and it has the potential to become a compelling therapeutic target for autoimmune conditions such as ITP[1,2]
- Ianalumab is an investigational, fully human, anti–BAFF-R monoclonal antibody with a dual mechanism of action[3–5]
- The VAYHIT3 study (NCT05885555) evaluates the safety and efficacy of ianalumab in patients with primary ITP treated with ≥2 prior lines of therapy
- We herein present the results of the primary analysis, which was conducted when all patients completed the Week 25 visit or discontinued earlier




ADCC, antibody-dependent cellular cytotoxicity; BAFF, B-cell–activating factor; BAFF-R, BAFF receptor; ITP, immune thrombocytopenia; NK, natural killer.

1. Emmerich F, et al. *Br J Haematol.* 2006;136:309–14; 2. Zhou Z, et al. *Autoimmunity.* 2009;42:112–9; 3. McWilliams EM, et al. *Blood.* 2013;122:4185; 4. Dörner T, et al. *Ann Rheum Dis.* 2019;78:641–7; 5. McWilliams EM, et al. *Blood Adv.* 2019;3:447–60.



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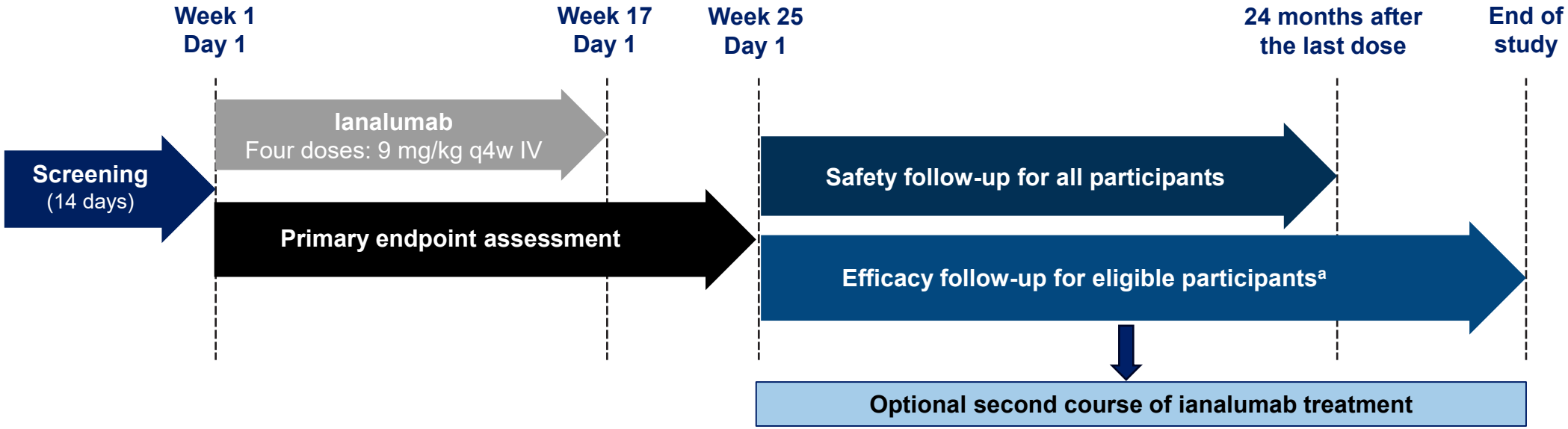
# Phase 2 VAYHIT3 study design

- Adults with primary ITP previously treated with at least a corticosteroid (+/-IVIG) and a TPO-RA, with no previous splenectomy
- Loss of response, no or insufficient response or intolerance to the last ITP therapy
- Platelet count of <30 G/L and assessed by the investigator as needing treatment

NCT05885555




**Data cutoff:** 5 Feb 2025

Participants were allowed to continue background corticosteroids and/or TPO-RA on which they had failed at the time of study entry. The dosage of the background treatment must have remained stable for a minimum of 14 days prior to initiating ianalumab and could not be increased once the study drug commenced.
Patients received premedication prior to the first 2 ianalumab infusions (paracetamol 1000 mg, antihistamine as per institutional guidelines and corticosteroid [prednisolone 50 mg or equivalent]).
[a]At Week 25 Day 1: platelet count of ≥30 G/L and ≥4 weeks since the last rescue and no new ITP treatment.
ITP, immune thrombocytopenia; IV, intravenous; IVIG, intravenous immunoglobulin; q4w, every 4 weeks; TPO-RA, thrombopoietin receptor agonist.



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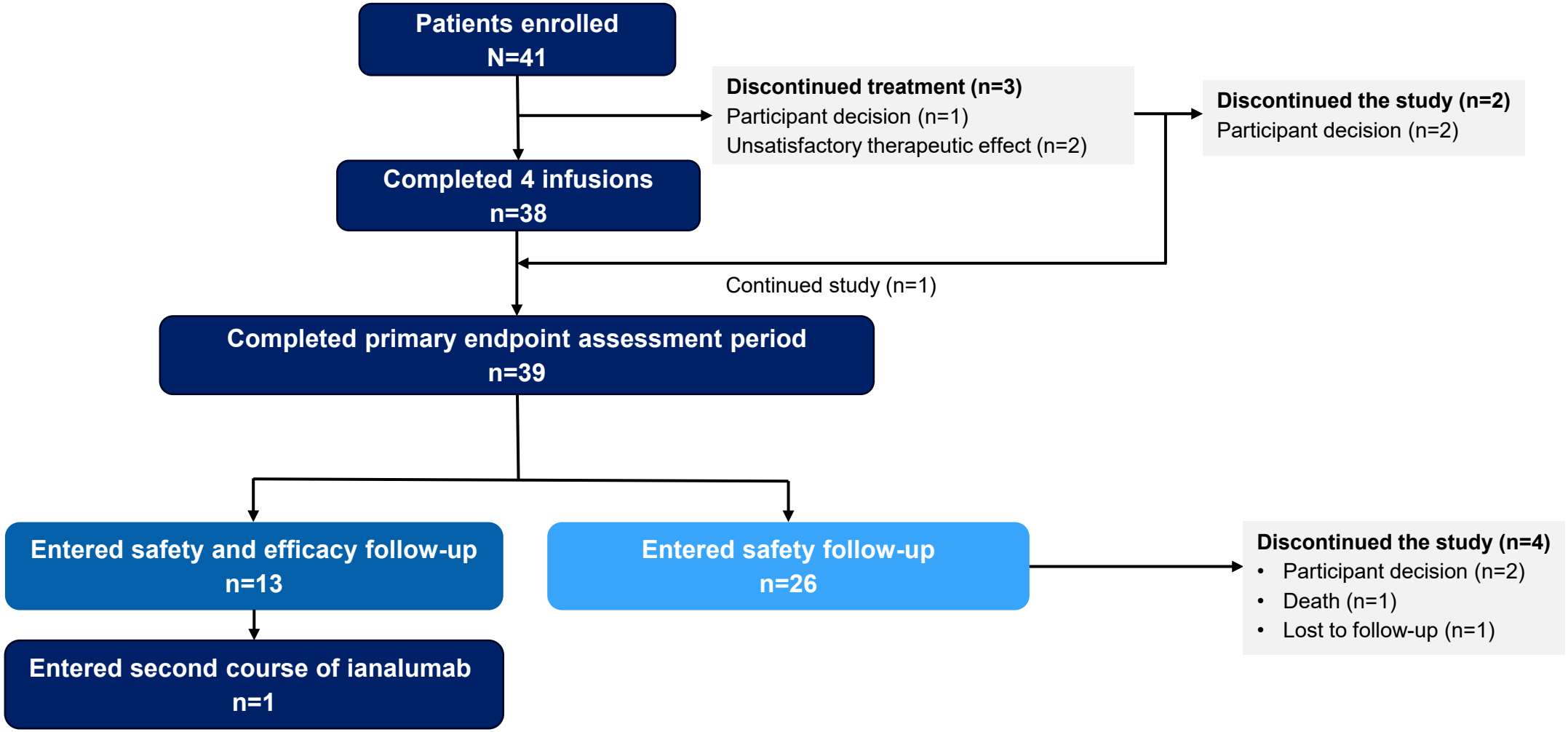
# Patient disposition



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# Patient demographics and baseline disease characteristics

| | Ianalumab N=41 |
|---|---|
| **Median age (range), years** | 55 (18–80) |
| **Male, n (%)** | 20 (49) |
| **Race, n (%)*** | |
| White | 32 (78) |
| Asian[a] | 8 (20) |
| **Ethnicity, n (%)*** | |
| Hispanic or Latino | 6 (15) |
| Not Hispanic or Latino | 34 (83) |
| **Median platelet count (range), G/L** | 8 (0–29) |
| **Median ITP duration (range), years[b]** | 4 (0–41) |

| | Ianalumab N=41 |
|---|---|
| **Median number of prior lines (range)** | 6 (2–13) |
| Prior lines ≥4, n (%) | 36 (88) |
| **Type of prior medications, n (%)** | |
| Corticosteroids | 41 (100) |
| TPO-RA | 41 (100) |
| IVIG or anti-D immune globulin | 33 (81) |
| Rituximab | 19 (46) |
| Other immunosuppressant[c] | 21 (51) |
| Other | 23 (56) |
| Fostamatinib | 10 (24) |

**Data cutoff:** 5 Feb 2025

*One patient had a missing race and ethnicity assessment.
[a]Includes Chinese (n=4), Korean (n=2), Indian (n=1) and other (n=1). [b]Time from the initial diagnosis of ITP was calculated from the date of initial diagnosis to the screening date.
[c]Azathioprine (n=10), cyclosporine (n=7), mycophenolic acid (n=12), sirolimus (n=2), tacrolimus (n=1) and vincristine (n=2).
ITP, immune thrombocytopenia; IVIG, intravenous immunoglobulin; TPO-RA, thrombopoietin receptor agonist.



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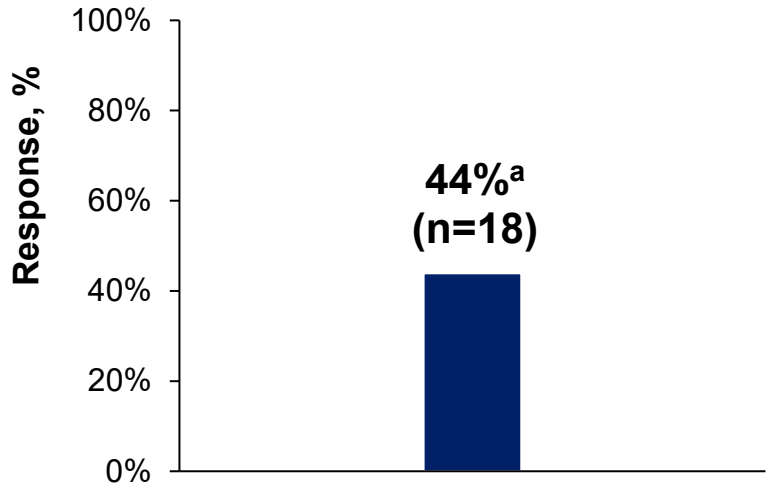
# Key efficacy endpoints

## Primary endpoint: Confirmed Response (ConfR)

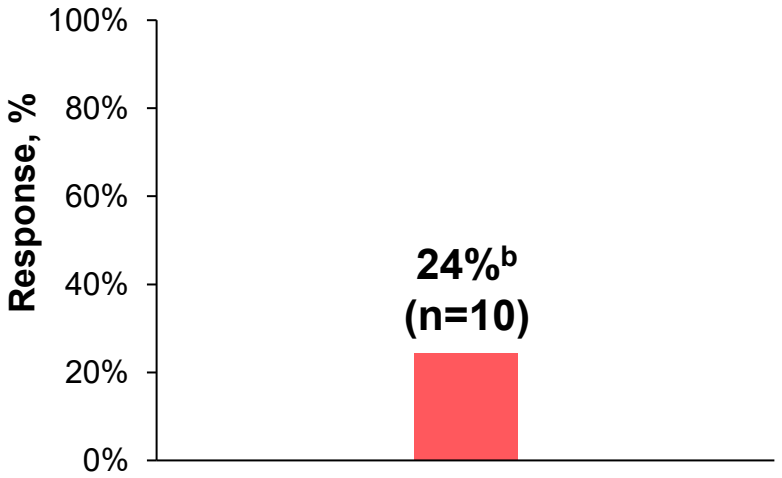
- Platelet count of ≥50 G/L at ≥2 consecutive assessments at least 7 days apart between Week 1 and Week 25
- No rescue therapy within ≥4 weeks of platelet count assessment or start of new therapy before ConfR




Median time to ConfR among responders: 6 weeks

## Stable Response (SR)

- Platelet count of ≥50 G/L on at least 75% of assessments between Week 19 and Week 25
- No rescue therapy within ≥4 weeks of platelet count assessment or start of new therapy before SR




10/18 (56%) responders achieved SR at Week 25, including 9 complete responses*

Among 18 participants with ConfR, 8 responded within the first month, 5 within the second month and 5 between 3 and 5 months.
*Complete response was defined as a platelet count of ≥100 G/L in the absence of rescue treatment or new ITP treatment.
[a]95% Bayesian credibility interval (30, 59); [b]95% confidence interval (12, 40).
ITP, immune thrombocytopenia.

**Data cutoff:** 5 Feb 2025



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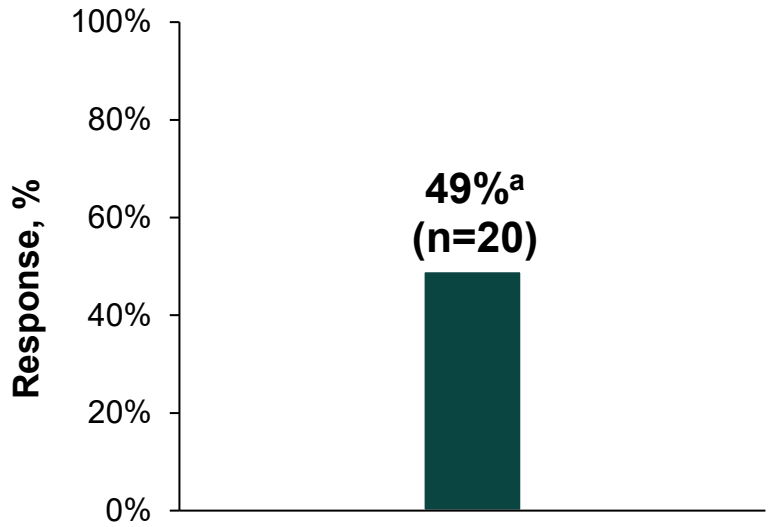
# Key efficacy endpoints (IWG criterion[1])

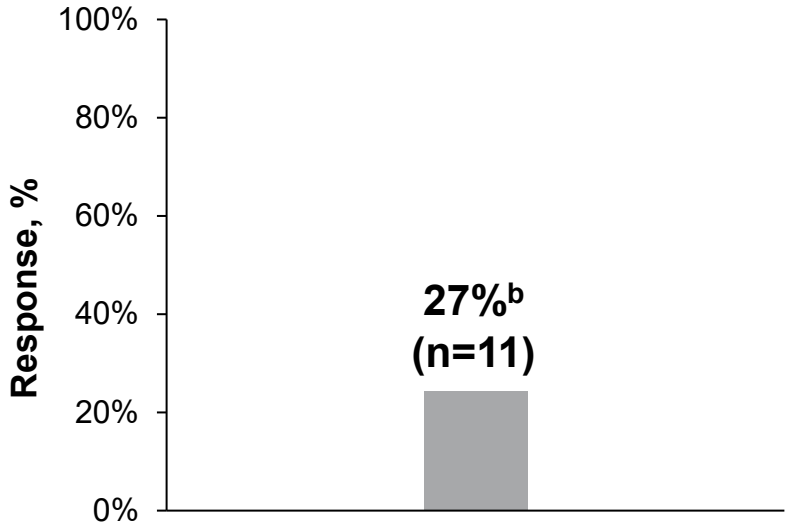
## IWG Confirmed Response (IWG-ConfR)

- Platelet count of **≥30 G/L** at ≥2 consecutive assessments at least 7 days apart between Week 1 and Week 25 **with at least a 2-fold increase from baseline**
- No rescue therapy within ≥4 weeks of platelet count assessment or start of a new therapy before ConfR




## IWG Stable Response (IWG-SR)

- Platelet count of **≥30 G/L** on at least 75% of assessments between Week 19 and Week 25 **with at least a 2-fold increase from baseline**
- No rescue therapy within ≥4 weeks of platelet count assessment or start of a new therapy before SR




**Data cutoff:** 5 Feb 2025

[a]95% Bayesian credibility interval for corresponding modified endpoints (34, 64); [b]95% confidence interval for corresponding modified endpoints (14, 43).
ConfR, confirmed response; IWG, International Working Group; SR, stable response.
1. Rodeghiero F, et al. *Blood*. 2009;113(11):2386-93.



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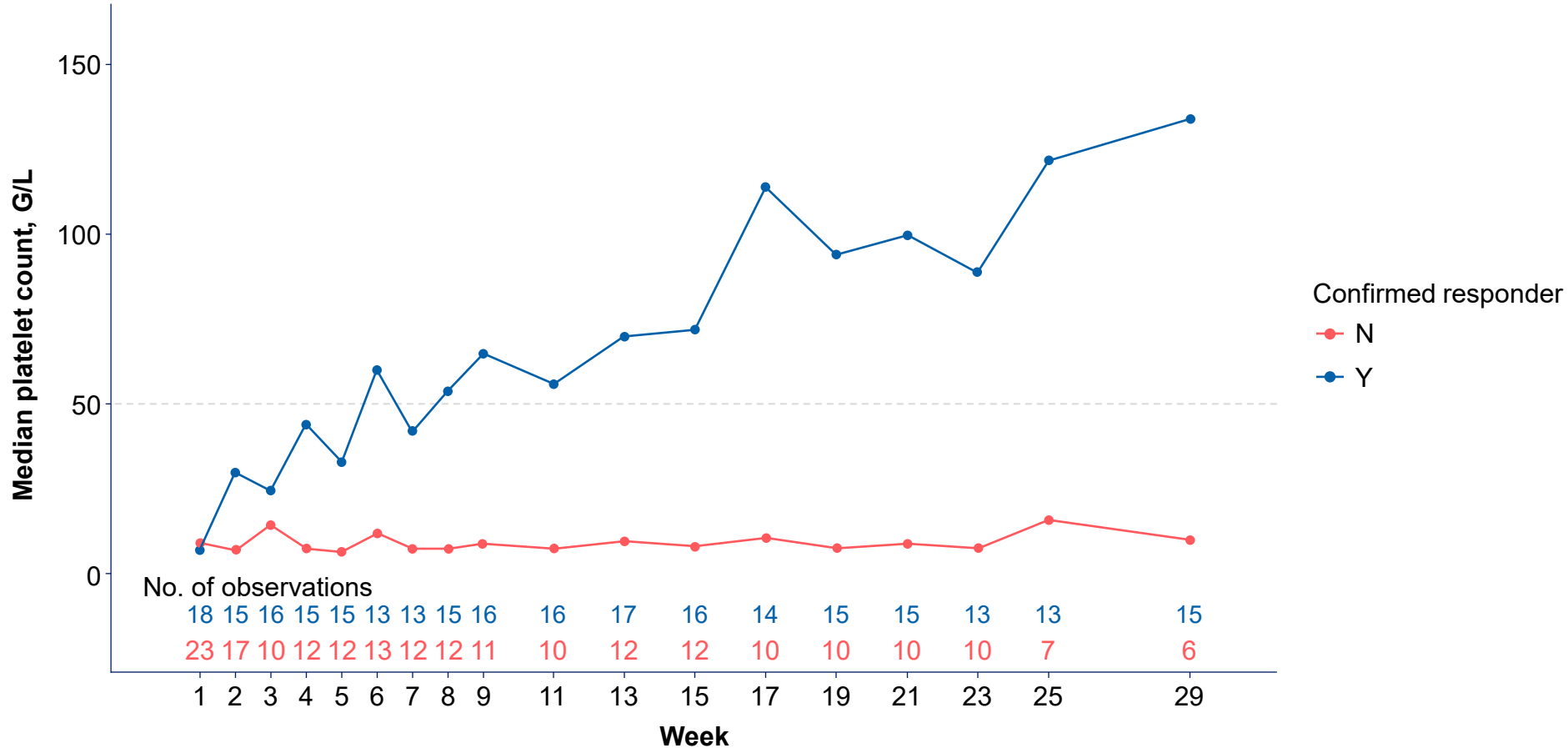
# Efficacy: Platelet count and bleeding events over time




- Rates of any-grade bleeding events (according to the WHO Bleeding Scale) decreased from 59% at baseline (n/N=24/41) to 22% at Week 25 (n/N=8/37) and 10% at Week 33 (n/N=3/30)

**Data cutoff:** 5 Feb 2025

Platelet counts collected within less than 4 weeks after the rescue treatment or after the start of a new ITP therapy were excluded for all post-baseline visits. Baseline is the worst value during the screening period or on the date the first course of ianalumab treatment started.
WHO, World Health Organization.



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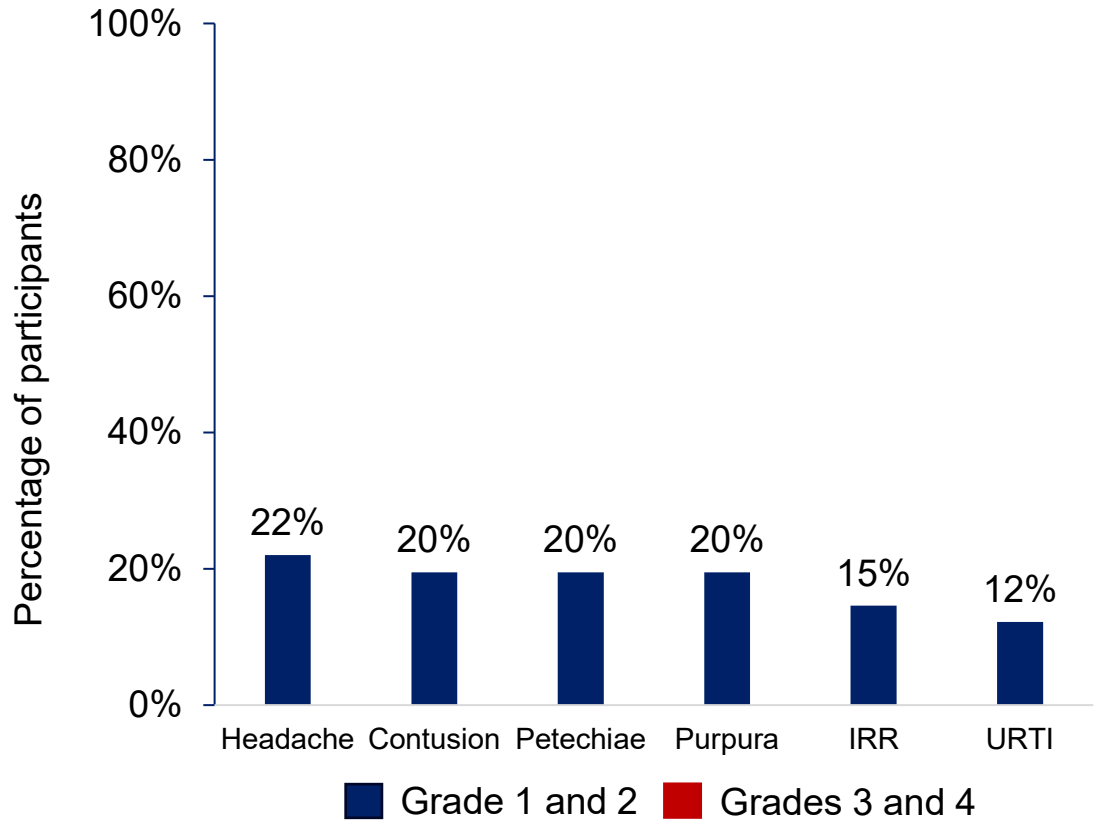
# Safety: Overview of on-treatment adverse events (AEs)

| Category | Ianalumab N=41 | |
|---|---|---|
| | All grades n (%) | Grade ≥3 n (%) |
| **AEs** | 35 (85) | 9 (22) |
| **Study drug-related** | 15 (37) | 1 (2) |
| **SAEs** | 6 (15) | 6 (15) |
| **Study drug-related** | 0 | 0 |
| **Fatal AEs** | 0 | 0 |
| **AEs leading to study treatment discontinuation** | 0 | 0 |

## Most frequent AEs (>10%)




**Data cutoff:** 5 Feb 2025

Note: No Grade ≥3 AEs were reported among the most frequently observed AEs.
On-treatment: AEs started during the period from the day of the first administration of the study drug to 28 days after the last administration of the study drug. Participants with multiple severity grades for an AE are counted only under the maximum grade. MedDRA version 27.1, CTCAE version 5.0.
CTCAE, Common Terminology Criteria for Adverse Events; IRR, infusion-related reaction; MedDRA, Medical Dictionary for Regulatory Activities; SAE, serious adverse event; URTI, upper respiratory tract infection.



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# Safety: On-treatment SAEs and AEs of special interest

## On-treatment SAEs

| Preferred term | Ianalumab (N=41) | |
|---|---|---|
| | All grades n (%) | Grades 3–4 n (%) |
| **Thrombocytopenia** | 2 (5) | 2 (5) |
| **Allergy to immunoglobulin therapy** | 1 (2) | 1 (2) |
| **Arterial disorder** | 1 (2) | 1 (2) |
| **Chronic kidney disease** | 1 (2) | 1 (2) |
| **Liver disorder** | 1 (2) | 1 (2) |
| **Upper gastrointestinal haemorrhage** | 1 (2) | 1 (2) |

**Data cutoff:** 5 Feb 2025

## AEs of special interest

- IRRs were reported in 6 participants (15%), all of which were Grade 1 or 2, with no discontinuations due to IRRs
- Infections were reported in 15 participants (37%); 1 (2%) participant experienced a Grade 3 infection (*Clostridium difficile* infection)

- One patient died in the post-treatment phase due to an AE of pulmonary oedema. The event was reported by the investigator as not related to ianalumab

Note: No Grade 5 AEs were reported.
SAEs occurring during treatment or within 28 days of the last dose of the study drug were considered in this analysis. A participant with multiple severity grades for an AE is counted only under the maximum grade. MedDRA version 27.1, CTCAE version 5.0.
AE, adverse event; CTCAE, Common Terminology Criteria for Adverse Events; IRR, infusion-related reaction; MedDRA, Medical Dictionary for Regulatory Activities; SAE, serious adverse event.



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# Conclusions

- The primary analysis of VAYHIT3 based on 41 patients provides preliminary results on the efficacy (as assessed during the first 25 weeks after treatment start) and tolerability of a short course of ianalumab administered intravenously in heavily pretreated patients with primary ITP, with no new safety signals detected up to the data cutoff
  - Nearly half (44%) of the patients achieved ConfR, with most experiencing it during the first 2 months, and more than half of the responders maintained a stable response at 6 months
  - There were no discontinuations due to AEs. IRRs and infections were of Grade 1 or 2, except one Grade 3 infection
- Ianalumab is currently being investigated in the ongoing Phase 3 studies VAYHIT1 (NCT05653349) and VAYHIT2 (NCT05653219) as first-line and second-line treatments for primary ITP, respectively

AE, adverse event; ConfR, confirmed response; IRR, infusion-related reaction; ITP, immune thrombocytopenia.



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